

**REMARKS**

The present application was filed on July 27, 2001, with 54 claims: method claims 1-50 and composition claims 51-54. On December 5, 2001, the Office mailed a Restriction Requirement and Species Election. On January 7, 2002, Applicants elected the claims of Group I (claims 1-45 and 50) and the species dihydrotestosterone (DHT) propionate (including 4-dihydrotestosterone propionate, 5 $\alpha$ -dihydrotestosterone propionate, and stanolone). The claims of Group I reading on the elected species were identified as claims 1-12, 16-18, and 20-45. In the Office Action under reply, claims 46-49 and 51-54 were withdrawn from consideration as drawn to a non-elected invention; claims 13-15 and 19 were withdrawn from consideration as being drawn to a non-elected species; and claims 1-12, 16-18, 20-45, and 50 were rejected as set forth below.

With the present Amendment, a slight change has been made to page 10 of the specification; specifically, a bracket has been added to the chemical formula at line 17. This change is of a minor typographical nature and adds no new matter to the application. In addition, claims 40-42 have been canceled, as have restricted-out claims 51-54. To more clearly define the invention, claim 1 has been amended to recite the claimed method as comprising administering an androgen as a first active agent and optionally administering a second active agent selected from the group consisting of vasoactive agents, rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors and other peptidyl drugs, selective androgen receptor modulators (SARMs), neuropeptides, amino acids, serotonin agonists, serotonin antagonists, calcium channel blockers, potassium channel openers, potassium channel blockers, non-androgenic steroids, and combinations thereof. Claims 25-29 and 43 have been amended in light of the amendment to claim 1. Claims 1 and 48-50 have also been amended to remove the language objected to by the Examiner.

With this amendment, then, claims 1, 25-29, 43, and 48-50 have been amended, claims 40-42 and 51-54 have been canceled, and new claim 55 has been added. Accordingly, claims 1-39, 43-50, and 55 are now pending. For the Examiner's convenience, all pending claims upon entry of this amendment are set forth in Appendix B.

**CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH:**

Claim 20 stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors were in possession of the claimed invention at the time the application was filed. This rejection is respectfully traversed.

The Examiner rejected claim 20 on the grounds that no criteria is set forth in the specification to define the “lipoidal carrier effective to enhance the oral bioavailability of the androgenic agent.” The Examiner further asserts that the skilled artisan could not ascertain the lipoidal carriers without undue experimentation. The Examiner’s rejection lacks merit for the following reason.

Provided with this Amendment, is a minor change to the paragraph at page 10 of the specification, lines 8-21 (the Examiner’s attention is directed to the first page of this Amendment and the first page of Appendix A of this Amendment); this paragraph specifically refers to the subject matter which the Examiner asserts is missing from the application. In this paragraph, it is provided that “other androgenic agents that have oral activity, and whose oral activity can be enhanced by admixture with a lipoidal vehicle, include those mentioned in U.S. Patent No. 4,147,783 to van der Vies.” The specification then sets forth, by way of example, several esters of testosterone and DHT whose oral activity would be enhanced with a lipoidal carrier (see specification, page 10, lines 11-17). Immediately following this list of esters of testosterone and DHT whose oral activity would be enhanced with a lipoidal carrier is a list of “[s]uitable lipoidal vehicles for enhancing the oral activity of the aforementioned esters” (specification, page 10, lines 17-21). Based upon this disclosure in the specification, it is clear the “lipoidal carrier effective to enhance the oral bioavailability of the androgenic agent” of claim 20 is fully supported by the written description of the present application.

Because the language of claim 20 is fully described in the specification in such as way as to reasonably convey to one of ordinary skill in the art that the inventors were in possession of the claimed subject matter at the time the application was filed, Applicants respectfully request reconsideration and withdrawal of this rejection.

**CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH:**

Claims 1-12, 16-18, 20-45, and 50 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner identifies the following language in claims 1 and 50 as forming the basis for this rejection: “regular dosing within the context of a chronic dosing regimen.” The Examiner states that this language is indefinite as to the dosing frequency of the agent encompassed by the claims and suggests removing this language. On this matter, the Examiner’s attention is directed to the fact that the independent claims in which the objected-to phrase was originally present are claims 1 and 48-50. While not wishing to acquiesce in the rejection, applicants have amended the aforementioned claims to remove the objected-to language and thereby expedite prosecution. Therefore, this rejection is now moot.

In addition to the foregoing, claim 20 was the subject of another indefiniteness rejection under 35 U.S.C. § 112, second paragraph. This rejection is respectfully traversed.

With this rejection, the Examiner again objects to the language "lipoidal carrier" as indefinite on the grounds that it is unclear what carriers are encompassed by the claims, which would enhance the bioavailability of the androgenic agents. As explained above in the traversal to the Examiner's 35 U.S.C. § 112, first paragraph, rejection over claim 20, the specification clearly defines what lipoidal carriers are encompassed by the claims. Further, the recitation in the specification that exemplary lipoidal carriers are set forth in the '783 Patent to van der Vies clearly demonstrates that lipoidal carriers that are capable of enhancing the bioavailability of certain androgenic agents are readily ascertainable to one of ordinary skill in the art. Accordingly, because the "lipoidal carriers" of claim 20 are clearly defined, Applicants respectfully request reconsideration and withdrawal of this rejection.

#### CLAIM REJECTIONS - 35 U.S.C. § 103

Claims 1-12, 16-18, 20-45, and 50 stand rejected under 35 U.S.C. § 103(a) as obvious over Adams et al. and Place et al. This rejection is respectfully traversed.

Adams et al. teaches means for diagnosing the presence or absence of sexual dysfunction in a female by administering apomorphine alone or in combination with an androgen and observing any change in physiology response associated with sexual activity: a change indicating the presence of sexual dysfunction (page 9, lines 15-22). To illustrate this method, Adams et al. use an animal model consisting of female Wistar rats. Adams et al. explain that the purpose of the androgen in the model set forth therein is to potentiate the sexual arousal effects of apomorphine in the female rats (page 20, lines 10-12 and page 21, lines 3-4). Under the animal model used in Adams et al., female Wistar rats were administered the apomorphine and androgen by injection in the back of their necks and then observed for symptoms of sexual arousal, i.e., yawning and genital licking (page 27, line 20 to page 28, line 5 and page 28, line 28 to page 29, line 8). Adams et al. explains that the yawning is a direct indication of central activation of dopaminergic receptors by apomorphine and that the genital licks are the analogous female rat response to penile erections in the male rat (page 27, lines 4-19). Adams et al. do *not* teach or suggest administration of the androgen alone or without the apomorphine. Further, because Adams et al. specifically identify the purpose of the androgen as *useful only to potentiate the sexual arousal effects of the apomorphine*, it follows that the role of the androgen in the Adams et al. animal model is not associated with the treatment of sexual dysfunction but rather, as a catalyst to improve the sexual arousal effects of the apomorphine. Based upon the foregoing, it is clear that there is no suggestion

in Adams et al. that the androgen may be useful *on its own* as a primary agent to treat female sexual dysfunction.

In support of the foregoing, applicants have amended claim 1 to recite that any secondary active agent is selected from the Markush group now set forth in part (b) of the claim. All of the recited active agents are vasoactive agents; the claim thus excludes other types of secondary agents such as apomorphine, disclosed by Adams et al. With respect to the remaining independent claims, Adams et al. neither discloses nor suggests the methods of claims 44 and 46-50, since Adams et al. does not disclose co-administration with a prostaglandin (claim 44), a method for improving tissue health of the female genitalia (claim 46), a method for preventing vaginal atrophy (claim 47), a method for preventing vaginal pain during sexual intercourse (claim 48), a method for alleviating vaginal itching and dryness (claim 49), or a method wherein the blood level of the androgenic agent or a metabolite thereof approximates the blood level of the agent or metabolite during ovulation (claim 50). In addition, new claim 55 recites that the method consists "essentially of orally administering ... an ... androgenic agent..." thus distinguishing over Adams et al.

Place et al. does not correct the deficiencies of Adams et al. The Place et al. reference relates to a method of treating sexual dysfunction in a female individual comprising administering to the vagina or vulvar area of the individual a pharmaceutical formulation comprising an effective amount of a vasodilating agent selected from the group consisting of naturally occurring prostaglandins, synthetic prostaglandin derivatives, pharmaceutically acceptable salts, esters, and inclusion complexes, and combinations thereof (claim 1). The entirety of Place et al. is focused on *local* drug administration, however; the reference does not contemplate *oral* drug administration. It is of course well established in the fields of pharmacotherapy and drug delivery that oral and local drug delivery are very different, involving different dosage forms, different manufacturing methods, different drugs, different doses, etc. One of ordinary skill in the art would not turn to a reference on local drug administration in developing an oral drug delivery system or a therapeutic method involving oral drug administration, as claimed herein.

Furthermore, because Place et al. provides no suggestion that the androgens taught therein may be administered *orally* and/or without a second active agent. Place et al. provides no motivation for one of ordinary skill in the art to modify the invention of Adams to orally administer an androgen, as needed, as the sole active agent for the treatment of female sexual dysfunction, or in combination with a vasoactive agent as recited in claim 1. Indeed, when the teachings of Adams et al. and Place et al. are placed side by side, the role of the androgen in both references is clearly that of a secondary agent to enhance the therapeutic properties of the apomorphine or the

prostaglandins disclosed therein, respectively. Accordingly, it is clear that the combination of Adams et al. and Place et al. does not result in the claimed invention.

Applicants accordingly respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

Applicants respectfully submit, in conclusion, that the present claims are patentable over the art and comply with all requirements of 35 U.S.C. § 112. In light of the foregoing, Applicants respectfully request withdrawal of all claim rejections and early passage of this application to issue.

The Examiner is invited to contact the undersigned at 650-330-0900 with questions or comments regarding this communication.

Respectfully submitted,

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**APPENDIX A**  
**AMENDMENTS TO THE SPECIFICATION AND CLAIMS**

**IN THE SPECIFICATION:**

Amend the specification on page 10, lines 8-21, as follows:

Other androgenic agents that have oral activity, and whose oral activity can be enhanced by admixture with a lipoidal vehicle, include those mentioned in U.S. Patent No. 4,147,783 to van der Vies, including, by way of example, the following esters of testosterone and DHT: decanoate, pentadecanoate, undecanoate, pelargonate, tridecanoate, palmitate, caprate, isocaprate,  $\alpha$ -methylcaprate,  $\beta$ -methylcaprate, laurate,  $\alpha$ -methylpelargonate,  $\beta$ -methylpelargonate,  $\beta,\beta$ -dimethylpelargonate,  $\beta$ -(p-methyl-cyclohexyl)propionate,  $\beta$ -(p-ethyl-cyclohexyl)-propionate,  $\beta$ -(cycloheptyl)-propionate,  $\alpha$ -methyl- $\beta$ -cyclohexyl-propionate,  $\beta$ -methyl- $\beta$ -cyclohexyl-propionate, cyclododecyl-carboxylate, adamantine-1'-carboxylate, adamant-1'-yl-acetate, methyl- $\beta$ -cyclohexyl-propionate, and  $\beta$ -(bicyclo-[2,2,2]-oct-1'-yl)-propionate esters. Suitable lipoidal vehicles for enhancing the oral activity of the aforementioned esters are oils, e.g., arachis oil, castor oil, sesame oil, linseed oil, soya bean oil, sunflower seed oil, olive oil, fish liver oil, ethyl oleate, oleyl oleate, glyceryl trioleate, glyceryl dioleate, glyceryl monooleate, and oleic acid.

**IN THE CLAIMS:**

Amend claims 1, 25-29, 43, and 48-50 as follows:

1. (Amended) A method for enhancing sexual desire and responsiveness in a female individual, comprising: (a) orally administering to the individual a therapeutically effective amount of an orally active androgenic agent as a first active agent; and optionally (b) administering to the individual a therapeutically effective amount of a second active agent selected from the group consisting of vasoactive agents, rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors and other peptidyl drugs, selective androgen receptor modulators (SARMs), neuropeptides, amino acids, serotonin agonists, serotonin antagonists, calcium channel blockers, potassium channel openers, potassium channel blockers, non-androgenic steroids, and combinations thereof, wherein administration is on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

25. (Amended) The method of claim 1, ~~further comprising administering a~~ wherein the therapeutically effective amount of at least one additional the second active agent is administered.

26. (Amended) The method of claim 25, wherein the ~~at least one additional~~ second active agent is administered with the androgenic agent.

27. (Amended) The method of claim 25, wherein the ~~at least one additional~~ second active agent is administered prior to administration of the androgenic agent.

28. (Amended) The method of claim 25, wherein the ~~at least one additional~~ second active agent is administered after administration of the androgenic agent.

29. (Amended) The method of claim 25, wherein the ~~at least one additional~~ second active agent is a vasoactive agent.

43. (Amended) The method of claim 25, wherein administration of the ~~at least one additional~~ second active agent is topical, transdermal, sublingual, intranasal, buccal, rectal, parenteral, or by inhalation.

48. (Amended) A method for preventing vaginal pain during sexual intercourse, comprising orally administering to a female individual suffering from dyspareunia a therapeutically effective amount of an orally active androgenic agent on an as-needed basis ~~without regular dosing within the context of a chronic dosage regimen.~~

49. (Amended) A method for alleviating vaginal itching and dryness, comprising orally administering to a female individual in need of such treatment a therapeutically effective amount of an orally active androgenic agent on an as-needed basis ~~without regular dosing within the context of a chronic dosage regimen.~~

50. (Amended) A method for enhancing sexual desire and responsiveness in a female individual, comprising orally administering an orally active androgenic agent to the individual in an amount effective to provide a blood level of the agent or a metabolite thereof that approximates the blood level of the agent

or a metabolite thereof during ovulation, wherein said administering is carried out on an as-needed basis  
~~without regular dosing within the context of a chronic dosage regimen.~~

**APPENDIX B**  
**PENDING CLAIMS UPON ENTRY OF THIS AMENDMENT**

1. A method for enhancing sexual desire and responsiveness in a female individual, comprising:  
(a) orally administering to the individual a therapeutically effective amount of an orally active androgenic agent as a first active agent; and optionally administering to the individual a therapeutically effective amount of a second active agent selected from the group consisting of vasoactive agents, rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors and other peptidyl drugs, selective androgen receptor modulators (SARMs), neuropeptides, amino acids, serotonin agonists, serotonin antagonists, calcium channel blockers, potassium channel openers, potassium channel blockers, non-androgenic steroids, and combinations thereof, wherein administration is on an as-needed basis.
2. The method of claim 1, wherein the androgenic agent is contained within an oral dosage form.
3. The method of claim 2, wherein the pharmaceutical formulation is comprised of an immediate release dosage form, and the androgenic agent is administered about 0.25 to 72 hours prior to sexual activity.
4. The method of claim 3, wherein the androgenic agent is administered about 0.5 to 48 hours prior to anticipated sexual activity.
5. The method of claim 4, wherein the androgenic agent is administered about 1 to 24 hours prior to anticipated sexual activity.
6. The method of claim 5, wherein the androgenic agent is administered about 1 to 12 hours prior to anticipated sexual activity.
7. The method of claim 6, wherein the androgenic agent is administered about 1 to 4 hours prior to anticipated sexual activity.
8. The method of claim 2, wherein the pharmaceutical formulation is comprised of a sustained release dosage form.

9. The method of claim 8, wherein following administration, the sustained release dosage form provides release of the androgenic agent over a drug delivery period in the range of about 4 to 72 hours.
10. The method of claim 9, wherein the drug delivery period is in the range of about 4 to 48 hours.
11. The method of claim 10, wherein the drug delivery period is in the range of about 4 to 24 hours.
12. The method of claim 2 wherein the androgenic agent is selected from the group consisting of orally active testosterone esters, orally active dihydrotestosterone esters, methyl testosterone, dehydroepiandrosterone, and combinations thereof.
13. The method of claim 12, wherein the androgenic agent is an orally active testosterone ester.
14. The method of claim 13, wherein the orally active testosterone ester is selected from the group consisting of testosterone propionate, testosterone undecanoate, and testosterone C<sub>4</sub>-C<sub>6</sub> alkyl-substituted cycloalkylcarboxylates.
15. The method of claim 14, wherein the orally active testosterone ester is testosterone propionate.
16. The method of claim 12, wherein the androgenic agent is an orally active dihydrotestosterone ester.
17. The method of claim 16, wherein the orally active dihydrotestosterone ester is selected from the group consisting of dihydrotestosterone propionate, dihydrotestosterone undecanoate, and dihydrotestosterone C<sub>4</sub>-C<sub>6</sub> alkyl-substituted cycloalkylcarboxylates.
18. The method of claim 17, wherein the orally active dihydrotestosterone ester is dihydrotestosterone propionate.

19. The method of claim 12, wherein the androgenic agent is selected from the group consisting of testosterone decanoate, testosterone pentadecanoate, testosterone undecanoate, testosterone pelargonate, testosterone tridecanoate, testosterone palmitate, testosterone caprate, testosterone isocaprate, testosterone  $\alpha$ -methylcaprate, testosterone  $\beta$ -methylcaprate, testosterone laurate, testosterone  $\alpha$ -methylpelargonate, testosterone  $\beta$ -methylpelargonate, testosterone  $\beta,\beta$ -dimethylpelargonate, testosterone  $\beta$ -(p-methyl-cyclohexyl)propionate, testosterone  $\beta$ -(p-ethyl-cyclohexyl)-propionate, testosterone  $\beta$ -(cycloheptyl)-propionate, testosterone  $\alpha$ -methyl- $\beta$ -cyclohexyl propionate, testosterone  $\beta$ -methyl- $\beta$ -cyclohexyl propionate, testosterone cyclododecylcarboxylate, testosterone adamantine-1'-carboxylate, testosterone adamant-1'-yl-acetate, testosterone methyl- $\beta$ -cyclohexyl propionate, testosterone  $\beta$ -(bicyclo-[2,2,2-oct-1'-yl)-propionate, dihydrotestosterone decanoate, dihydrotestosterone pentadecanoate, dihydrotestosterone undecanoate, dihydrotestosterone pelargonate, dihydrotestosterone tridecanoate, dihydrotestosterone palmitate, dihydrotestosterone caprate, dihydrotestosterone isocaprate, dihydrotestosterone  $\alpha$ -methylcaprate, dihydrotestosterone  $\beta$ -methylcaprate, dihydrotestosterone laurate, dihydrotestosterone  $\alpha$ -methylpelargonate, dihydrotestosterone  $\beta$ -methylpelargonate, dihydrotestosterone  $\beta,\beta$ -dimethylpelargonate, dihydrotestosterone  $\beta$ -(p-methyl-cyclohexyl)propionate, dihydrotestosterone  $\beta$ -( $\beta$ -ethyl-cyclohexyl)-propionate, dihydrotestosterone  $\beta$ -(cycloheptyl)-propionate, dihydrotestosterone  $\alpha$ -methyl- $\beta$ -cyclohexyl propionate, dihydrotestosterone  $\beta$ -methyl- $\beta$ -cyclohexyl propionate, dihydrotestosterone cyclododecylcarboxylate, dihydrotestosterone adamantine-1'-carboxylate, dihydrotestosterone adamant-1'-yl-acetate, dihydrotestosterone methyl- $\beta$ -cyclohexyl propionate, dihydrotestosterone  $\beta$ -(bicyclo-[2,2,2-oct-1'-yl)-propionate, and combinations thereof.

20. The method of claim 19, wherein the dosage form further includes a lipoidal carrier effective to enhance the oral bioavailability of the androgenic agent.

21. The method of claim 1, wherein the therapeutically effective amount is in the range of about 1  $\mu$ g to about 250 mg.

22. The method of claim 21, wherein the therapeutically effective amount is in the range of about 1  $\mu$ g to about 150 mg.

23. The method of claim 22, wherein the therapeutically effective amount is in the range of about 10  $\mu$ g to about 100 mg.

24. The method of claim 2, wherein the therapeutically effective amount of the androgenic agent in the dosage form is a unit dosage.
25. The method of claim 1, wherein the therapeutically effective amount of the second active agent is administered.
26. The method of claim 25, wherein the second active agent is administered with the androgenic agent.
27. The method of claim 25, wherein the second active agent is administered prior to administration of the androgenic agent.
28. The method of claim 25, wherein the second active agent is administered after administration of the androgenic agent.
29. The method of claim 25, wherein the second active agent is a vasoactive agent.
30. The method of claim 29, wherein the vasoactive agent is a vasodilator.
31. The method of claim 30, wherein the vasodilator is selected from the group consisting of vasoactive prostaglandins, endothelin-derived relaxation factors, vasoactive intestinal polypeptide agonists, smooth muscle relaxants, leukotriene inhibitors, and pharmacologically active salts, esters, prodrugs, and metabolites thereof, and combinations of any of the foregoing.
32. The method of claim 31, wherein the vasodilator is a vasoactive prostaglandin.
33. The method of claim 32, wherein the vasoactive prostaglandin is selected from the group consisting of naturally occurring prostaglandins, semisynthetic prostaglandins, synthetic prostaglandins, and pharmaceutically acceptable, pharmacologically active salts, esters, amides, inclusion complexes, prodrugs, metabolites, and analogs thereof, and combinations of any of the foregoing.
34. The method of claim 33, wherein the vasoactive prostaglandin is selected from the group consisting of naturally occurring prostaglandins and hydrolyzable lower alkyl esters thereof.

35. The method of claim 34, wherein the vasoactive prostaglandin is selected from the group consisting of PGE<sub>0</sub>, PGE<sub>1</sub>, 19-hydroxy-PGE<sub>1</sub>, PGE<sub>2</sub>, 19-hydroxy-PGE<sub>2</sub>, PGA<sub>1</sub>, 19-hydroxy-PGA<sub>1</sub>, PGA<sub>2</sub>, 19-hydroxy-PGA<sub>2</sub>, PGB<sub>1</sub>, 19-hydroxy-PGB<sub>1</sub>, PGB<sub>2</sub>, 19-hydroxy-PGB<sub>2</sub>, PGB<sub>3</sub>, PGD<sub>2</sub>, PGF<sub>1α</sub>, PGF<sub>2α</sub>, PGE<sub>3</sub>, PGF<sub>3α</sub>, PGI<sub>2</sub>, and hydrolyzable lower alkyl esters thereof.

36. The method of claim 35, wherein the vasoactive prostaglandin is selected from the group consisting of PGE<sub>0</sub>, PGE<sub>1</sub>, PGE<sub>2</sub>, and the methyl, ethyl and isopropyl esters thereof.

37. The method of claim 32, wherein the vasoactive prostaglandin is selected from the group consisting of arboprostil, carbaprostacyclin, carboprost tromethamine, dinoprost tromethamine, dinoprostone, enprostil, iloprost, lipoprost, gemeprost, metenoprost, sulprostone, tiaprost, viprostil, viprostil methyl ester, 16,16-dimethyl-Δ<sup>2</sup>-PGE<sub>1</sub> methyl ester, 15-deoxy-16-hydroxy-16-methyl-PGE<sub>1</sub> methyl ester, 16,16-dimethyl-PGE<sub>1</sub>, 11-deoxy-15-methyl-PGE<sub>1</sub>, 16-methyl-18,18,19,19-tetrahydro-carbacyclin, 16(RS)-15-deoxy-16-hydroxy-16-methyl-PGE<sub>1</sub> methyl ester, (+)-4,5-didehydro-16-phenoxy-α-tetranor-PGE<sub>2</sub> methyl ester, 11-deoxy-11α,16,16-trimethyl-PGE<sub>2</sub>, (+)-11α,16α,16β-dihydroxy-1,9-dioxo-1-(hydroxymethyl)-16-methyl-trans-prostene, 9-chloro-16,16-dimethyl-PGE<sub>2</sub>, -16,16-dimethyl-PGE<sub>2</sub>, 15(S)-15-methyl-PGE<sub>2</sub>, 9-deoxy-9-methylene-16,16-dimethyl-PGE<sub>2</sub>, potassium salt, 19(R)-hydroxy-PGE<sub>2</sub>, 11-deoxy-16,16-dimethyl-PGE<sub>2</sub>, and combinations thereof.

38. The method of claim 32, wherein the therapeutically effective amount of the vasodilator is in the range of approximately 1 to 5000 μg.

39. The method of claim 38, wherein the therapeutically effective amount of the vasodilator is in the range of approximately 20 to 2000 μg.

43. The method of claim 25, wherein administration of the second active agent is topical, transdermal, sublingual, intranasal, buccal, rectal, parenteral, or by inhalation.

44. A method for enhancing sexual desire and responsiveness in a female individual, comprising orally administering to the individual, approximately 0.25 to 72 hours prior to sexual activity, a therapeutically effective amount of an orally active androgenic agent, followed by topical administration,

approximately 0.25 to 24 hours prior to sexual activity, of a therapeutically effective amount of a prostaglandin.

45. The method of claim 44, wherein the prostaglandin is selected from PGE<sub>0</sub>, PGE<sub>1</sub>, PGE<sub>2</sub>, and hydrolyzable lower alkyl esters thereof.

46. A method for maintaining improving the tissue health of the female genitalia, comprising orally administering to a female individual a therapeutically effective amount of an orally active androgenic agent on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

47. A method for preventing vaginal atrophy, comprising orally administering to a female individual a therapeutically effective amount of an orally active androgenic agent on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

48. A method for preventing vaginal pain during sexual intercourse, comprising orally administering to a female individual suffering from dyspareunia a therapeutically effective amount of an orally active androgenic agent on an as-needed basis.

49. A method for alleviating vaginal itching and dryness, comprising orally administering to a female individual in need of such treatment a therapeutically effective amount of an orally active androgenic agent on an as-needed basis.

50. A method for enhancing sexual desire and responsiveness in a female individual, comprising orally administering an orally active androgenic agent to the individual in an amount effective to provide a blood level of the agent or a metabolite thereof that approximates the blood level of the agent or a metabolite thereof during ovulation, wherein said administering is carried out on an as-needed basis.

55. A method for enhancing sexual desire and responsiveness in a female individual, consisting essentially of orally administering to the individual a therapeutically effective amount of an orally active androgenic agent on an as-needed basis.